REMARKS/ARGUMENTS

Claims 88-185 were pending. By virtue of the present amendment, claims 91-97, 120-126, 131-137, 142-148, 153-159, 161, 165, 169, 172, 175, 178, 181 and 184 have been canceled. Therefore, claims 88-90, 98-119, 127-130, 138-141, 149-152, 160, 162-164, 166-168, 170, 171, 173, 174, 176, 177, 179, 180, 182, 183 and 185 are pending and at issue.

Claims Objections

Claims 89 and 117 have been objected to because the Examiner alleges that the language "polypeptide, peptide and protein" is repetitive. Applicant respectfully disagrees.

One skilled in the art understands that each of these terms is distinct from the other. A "peptide" is a short sequence of amino acids, a "polypeptide" consists of a longer sequence of amino acids, and a "protein" is a high molecular weight polypeptide. The Court in *In re O'Farrell*, 7 USPQ2d 1673 (Fed. Cir. 1988) also understood the distinction, having consulted standard textbooks in the fields of molecular biology and genetic engineering (*The Molecular Biology of the Cell* and *The Molecular Biology of the Gene*).

> The basic organization of all proteins is the same. Proteins are large polymeric molecules consisting of chains of smaller building blocks, called *amino acids*, that are linked together covalently. [Footnote omitted] The chemical bonds linking amino acids together are called *peptide* bonds, so proteins are also called *polypeptides*[3].
>
> [3]Proteins are often loosely called *peptides*, but technically proteins are only the larger peptides with chains of at least 50 amino acids, and more typically hundreds of amino acids. Some proteins consist of several polypeptide chains bound together covalently or noncovalently. The term "peptide" is broader than "protein" and also includes small chains of amino acids linked by peptide bonds, some as small as two amino acids. Certain small peptides have commercial or medical significance.

7 USPQ2d at 1674-75. Applicant submits that the terms "peptide," "polypeptide," and "protein" are not repetitive, but rather have distinct meanings to those skilled in the art. The objection is therefore improper and should be withdrawn.

Claims 105, 109, 160-161, 163-165 and 167 have been objected to because the Examiner alleges that they "are directed to a method of increasing the ability of an antigenic composition containing an HIV antigen to perform an immune stimulating task in a vertebrate host by administering to said host the antigenic composition," but "the claims do not require the elicitation of an immune response against the pathogen of interest in a host."

Claims 105, 109, 160, 163 and 167 have been amended to recite that the immune response elicited is against the pathogen of interest. Claims 161 and 165 have been canceled. Accordingly, this objection has been overcome and should be withdrawn.

Claims 109, 164, 165 and 167 have been objected to because the Examiner alleges that 'the recitation 'elicit cytotoxic T lymphocytes in a vertebrate' appears to be incomplete." The Examiner suggests amending the recitation to indicate that it is the elicitation of cytotoxic T lymphocyte response that is desired.

Claims 109, 164 and 167 have been amended to recite that cytotoxic T lymphocyte responses are elicited. Claim 165 has been canceled. Accordingly, this objection has been overcome and should be withdrawn.

Claim Rejections

35 USC § 112, second paragraph

Claims 98, 105, 109, 116-122, 125, 126, 160, 161, 163-165 and 167 stand rejected because the phrase "derived from" allegedly renders them indefinite. Applicant respectfully disagrees.

One of skill in the art understands that antigens may be obtained from biological sources such as bacteria, viruses, tumor cells or fungi by many alternative methods. It is well known in the art that the protein may be directly purified from the pathogen itself

or from cells infected with the pathogen or in the case of tumors, from the tumor cells. One of skill in the art also understands that rather than purify the protein directly from infected cells, the gene encoding the antigen may be cloned and expressed in a more convenient culture system. Therefore the "derived from" language serves as a well-understood shorthand to reciting well-known steps.

Furthermore, the Patent Office has regularly accepted the phrase "derived from." See, for example, U.S. Patent No. 6,544,518, claim 9 ("An immunogenic composition as claimed in claim 8, wherein said antigen is derived from an organism . . . ."), and U.S. Patent No. 6,406,705, claim 9 ("The composition of claim 8, wherein the antigen is derived from an infectious agent selected from the group consisting of a virus, bacterium, fungus and parasite.").

Since one of skill in the art would indeed understand the meaning of "derived from" and the Patent Office regularly accepts such terminology, Applicant submits that this rejection is improper and should be withdrawn.

Regarding claims 105 and 109, the recitation "selected antigen" also allegedly renders them indefinite. To overcome this rejection, Applicant has deleted "selected" from these claims.

Regarding claims 105, 109, 160, 161, 163-165 and 167, the Examiner alleges that these claims are also indefinite because "it is unclear how the administration of the claimed antigenic composition would result in an increase in the ability of the antigenic composition to elicit an immune response, including cytotoxic T lymphocyte response, in a host."

Applicant points the Examiner to the paragraph bridging pages 6 and 7 of the specification:

> Adjuvants, cytokines and lymphokines are immune modulating compounds which have the ability to enhance and steer the development and profile of immune responses against various antigens that are themselves poorly immunogenic. The appropriate selection of adjuvants, cytokines and lymphokines can induce good humoral and cellular immune responses that would not develop in the absence of adjuvant, cytokine or lymphokine. In particular, adjuvants, cytokines and lymphokines have significant effects in enhancing the immune response to subunit and peptide antigens in vaccines. Their stimulatory activity is also

> beneficial to the development of antigen-specific immune responses directed against protein antigens. For a variety of antigens that require strong mucosal responses, high serum titers, induction of CTL and vigorous cellular responses, adjuvant and cytokine/lymphokine combinations provide stimuli that are not provided by most antigen preparations.

Applicant has combined a powerful adjuvant (MPL), as a soluble or stable oil-in-water emulsion (SE), with the cytokine GM-CSF and with the lymphokine IL-12; GM-CSF and IL-12 each act as adjuvants. Both adjuvant combinations (MPL + GM-CSF and MPL + IL-12) increase the claimed antigenic composition's ability to elicit an immune response.

35 USC § 102(a)

Claims 88-90 and 96-97 stand rejected as allegedly being anticipated by Boon et al., WO 98/57659. Applicant traverses this rejection.

Claim 88 as amended is directed to an antigenic composition *consisting of* an antigen and an effective adjuvanting amount of the combination of: (1) 3-O-deacylated monophosphoryl lipid A or monophosphoryl lipid A, and (2) a cytokine or lymphokine selected from the group consisting of granulocyte macrophage colony stimulating factor (GM-CSF) and interleukin-12 (IL-12), together with a diluent or carrier.

Boon et al., on the other hand, are concerned with identifying the cytokine that would best augment the already known adjuvant combination of MPL and the saponin QS-21. Throughout the disclosure, Boon et al. refer only to a three-adjuvant combination that contains IL-12, MPL and QS-21. Boon et al. do not teach or suggest adding IL-12 to MPL in the absence of QS-21. Nor do Boon et al. teach that GM-CSF is a possible component of the adjuvant combination. Rather, Boon et al. teach that GM-CSF was "unable to enhance the effect of the QS21/MPL adjuvant." (Page 3, lines 16-17). Consequently, since every element of the presently claimed invention is not identically shown in Boon et al., the claimed invention cannot be anticipated by this reference. Applicant therefore requests that this rejection be withdrawn.

35 USC § 103(a)

Claims 98, 116, 117, 119, 125 and 126 stand rejected as being obvious over Boon et al., WO 98/57659, as applied to claims 88, 90, 96 and 97 above. Applicant traverses the rejection.

Claims 98, 116, 117, 119 and 126 depend directly or indirectly from independent claim 88. Claim 126 has been canceled. Claim 88 as amended is directed to an antigenic composition *consisting of* an antigen and an effective adjuvanting amount of the combination of: (1) 3-O-deacylated monophosphoryl lipid A or monophosphoryl lipid A, and (2) a cytokine or lymphokine selected from the group consisting of granulocyte macrophage colony stimulating factor (GM-CSF) and interleukin-12 (IL-12), together with a diluent or carrier. The dependent claims recite that the antigen is derived from a pathogenic virus (claim 98), particularly HIV (claims 116-117), and that the 3-O-deacylated monophosphoryl lipid A in the composition of claim 116 is used in the form of a stable oil-in-water emulsion (claim 119).

Boon et al. are concerned with identifying the cytokine that would best augment the already known adjuvant combination of MPL and the saponin QS-21. Throughout the disclosure, Boon et al. refer only to a three-adjuvant combination that contains IL-12, MPL and QS-21. Boon et al. do not teach or suggest adding IL-12 to MPL in the absence of QS-21. Nor do Boon et al. teach that GM-CSF is a possible component of the adjuvant combination. Rather, Boon et al. teach that GM-CSF was "unable to enhance the effect of the QS21/MPL adjuvant." (Page 3, lines 16-17) As such, Boon et al. teach away from the presently claimed invention. Boon et al. clearly fail to appreciate and describe the useful two-adjuvant combination of the present invention. Applicant requests that this rejection be withdrawn.

Claims 105, 109, 160, 161, 163-165 and 167 stand rejected as being obvious over Boon et al., WO 98/57659, as applied to claims 88, 98, 116, 125 and 126 above. Applicant traverses the rejection.

Claims 105, 109, 160, 163, 164 and 167 depend directly or indirectly from independent claim 88. Claims 161 and 165 have been canceled. Claim 88 as amended is directed to an antigenic composition *consisting of* an antigen and an effective adjuvanting amount of the combination of: (1) 3-O-deacylated monophosphoryl lipid A or monophosphoryl lipid A, and (2) a cytokine or lymphokine selected from the group consisting of granulocyte macrophage colony stimulating factor (GM-CSF) and interleukin-12 (IL-12). Dependent claims 105, 160 and 163 recite the administration of the antigenic composition of claim 98 (wherein the antigen is from a pathogenic virus) to a vertebrate host to elicit an immune response in the host. Dependent claims 109, 164

and 167 recite the administration of the antigenic composition of claim 98 to a vertebrate host to elicit cytotoxic T lymphocyte responses in the host.

As Applicant pointed out above, Boon et al. disclose an adjuvant composition comprising not less than three adjuvants: a saponin adjuvant, monophosphoryl lipid A or a derivative thereof, and IL-12. In particular, Boon et al.'s adjuvant composition comprises QS21, 3-O-deacylated monophosphoryl lipid A (3D-MPL), and IL-12. Boon et al.'s composition would not contain GM-CSF because they found that it was "unable to enhance the effect of the QS21/MPL adjuvant." Therefore, the skilled artisan who combines Boon et al.'s three-adjuvant composition with an antigen to elicit an immune response or cytotoxic T lymphocyte responses does not arrive at the present invention as now claimed, which requires the use of a two-adjuvant composition (3D-MPL + GM-CSF or 3D-MPL + IL-12) together with an antigen from a pathogenic virus.

Applicant requests that this rejection be withdrawn.

Claim 118 stands rejected as being obvious over Boon et al., WO 98/57659, in view of Haynes et al., U.S. Patent No. 5,993,819 ("the Haynes '819 patent"), as being applied to claims 88, 98, 116 and 117 above. Applicant traverses the rejection.

Claim 118, which depends indirectly from claim 88 provided above, recites that the antigen is the HIV peptide having the amino acid sequence of either SEQ ID NO:1 or SEQ ID NO:2.

Boon et al. teach the three-adjuvant composition described above, which can be combined with an antigen, such as an HIV antigen, to elicit an immune response against that antigen. The Haynes '819 patent teaches an antigen having a sequence that is 100% identical to that of claimed SEQ ID NO:2. The Examiner takes the position that one of ordinary skill in the art would have been motivated to use the antigen of the Haynes '819 patent with the adjuvant composition of Boon et al. to make an antigenic composition for use in HIV treatment. The Examiner further alleges that one skilled in the art at the time the invention was made would have had a reasonable expectation of success for making the claimed invention.

Even if one skilled in the art were motivated to combine the antigen of the Haynes '819 patent with the adjuvant composition of Boon et al., and had a reasonable expectation of succeeding, the skilled artisan would still fall short of obtaining the presently claimed invention – an antigenic composition consisting of the HIV peptide

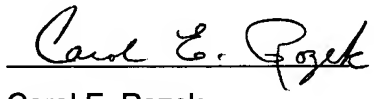
having SEQ ID NO:2 together with a specific two-adjuvant composition (3D-MPL + GM-CSF or 3D-MPL + IL-12). Thus, the claimed invention is not *prima facie* obvious.

Claims 91-93 and 120-122 stand rejected as being obvious over Boon et al., WO 98/57659, as applied to claims 88, 90, 98 and 116 above, in further view of Whittle et al., U.S. Patent No. 5,955,087.

The cancellation of claims 91-93 and 120-122 renders this rejection moot, and therefore, this rejection should be withdrawn.

In view of the above amendments and remarks, Applicant submits that the present application is in condition for allowance, and a Notice to that effect is requested.

Respectfully submitted,



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